Exploring Cognitive and Neuroanatomical Trajectories in Dementia: A Longitudinal MRI Study

Xiaojing Liu (#1004263888)

1. Introduction

Dementia is one of the most serious challenges in neurodegenerative diseases, presenting intricate dilemmas to clinicians and researchers alike. Due to its elusive nature, it is necessary to understand its progress from multiple perspectives. This report delves into a longitudinal MRI study comparing demented and non-demented patients, providing insight into the evolution of cognitive and anatomical markers over time. The report provides a thorough quantitative analysis on the patient with and without dementia, on the cognitive and neuroanatomical abilities using mixed effect ANOVA (within and between subjects across multiple visits) and statistical power analysis. There are two models in this report.

To untangle the cognitive and neuroanatomical abilities of the patients with/without dementia, this report will focus on two core research questions.

1. How does cognitive functioning, as quantified by the MMSE, vary over different visits within patients diagnosed with dementia compared to those without, when accounting for intra-individual variability?
2. Does the normalized Whole Brain Volume (nWBV) demonstrate a differential trajectory over multiple visits between the demented and non-demented groups, while controlling for individual differences?

2. Data cleaning and Data wrangling

As part of the analysis preparation steps, firstly, I checked the data for missing values or outliers. There was one missing value in the dependent variable MMSE, so I clean the missing value and called the cleaned dataset as df to ensure that won't influence the outcome.

3. Exploratory Data Analysis

1) Summary statistics for dependent variable MMSE by group

Visit	Group	mean	std
1	Converted	29.36	0.93
	Demented	25.33	3.32
	Nondemented	29.19	0.85
2	Converted	28.00	2.09
	Demented	24.25	4.40
	Nondemented	29.11	0.96

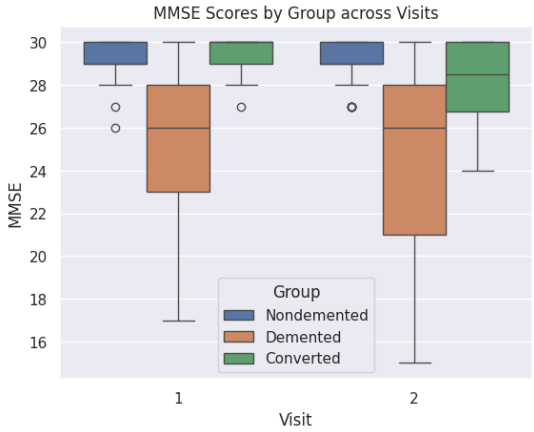
Interpretation: On the first visit, the Converted and Nondemented groups had very higher average scores. The Demented group's average score was significantly lower than the other two groups in both visits. The demented group has higher variability. By the second visit, the mean scores for all three groups decreased, and their standard deviations increased, which may suggest a decline in cognitive function and greater variability in the scores.

2) Summary Statistics for dependent variable nWBV by group

Visit	Group	mean	std
1	Converted	0.74	0.03
	Demented	0.72	0.03
	Nondemented	0.75	0.04
2	Converted	0.73	0.04
	Demented	0.71	0.03
	Nondemented	0.74	0.04

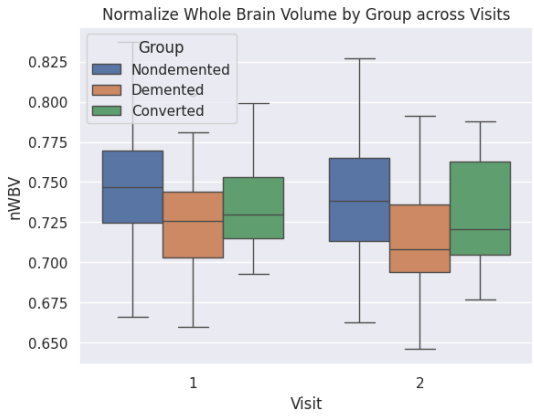
Interpretation: Generally, the mean of nWBV (normalized Whole Brain Volume) is quite similar among the three groups. The average of nWBV is highest for the nondemented group at both visits. The Demented group shows the lowest mean nWBV values at both visits. The nWBV of nondemented group has higher variability than that of demented group. The nWBV tends to decrease from Visit 1 to Visit 2 for all groups.

3) Data Visualization – Model 1 MMSE Scores by Group across visits



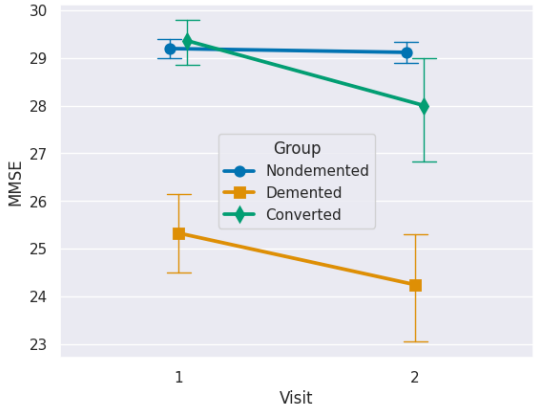
Interpretation: The Nondemented group's scores are high and tight, showing consistency in cognitive performance, albeit with a few outliers in the first visit. On the other hand, the Demented group's scores are relatively lower, with a wide range reflecting greater variability in cognitive abilities. This group does not present outliers. The Converted group serves as a middle ground. Across the two visits, all groups exhibit a downward shift in median MMSE scores, with the Nondemented and Converted groups also showing increased score variability, suggesting a potential overall decline in cognitive function over time.

4) Data Visualization – Model 2 nWBV Scores by Group across visits



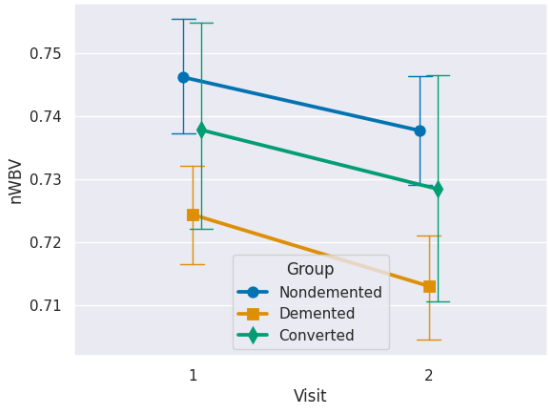
Interpretation: The median nWBV for each group shows a downward trend from the first to the second visit, indicating a general decrease in brain volume over time. The Nondemented and Converted groups exhibit a slight increase in the spread of their interquartile ranges from the first to the second visit. Meanwhile, the Demented group maintains a consistent interquartile range across the two visits. The plot does not show any outliers. This consistency across visits may reflect the regular progression of changes in brain volume associated with aging or disease in the studied population.

5) Data Visualization – MMSE score Trend Across Visits by Group line chart



Interpretation: The Nondemented group had high initial MMSE scores, which slightly declined by the second visit. In contrast, the Demented group started with much lower scores, deteriorating further over time. The Converted group's scores began in the middle but significantly fell by the second visit, highlighting a marked cognitive decline. Variability in MMSE scores, depicted by error bars, was minimal for the Nondemented group but notably higher for the Demented and Converted groups, indicating greater score fluctuation, particularly by the second visit.

6) Data Visualization – nWBV score Trend Across Visits by Group line chart



Interpretation: All groups show a decrease in nWBV from the first to the second visit, with the Converted group experiencing the largest decrease. Larger error bars for the Converted group on the second visit suggest greater variability in nWBV within this group at this time point.

4. Mixed Effect ANOVA

1) Model 1 MMSE Scores by Group across visits - Mixed Effect ANOVA

Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	1328.42	2	140	664.21	56.21	<0.001	0.445	nan
Visit	22.38	1	140	22.38	8.86	0.003	0.060	1.00
Interaction	17.00	2	140	8.50	3.37	0.037	0.046	nan

Interpretation: The group factor significantly affects the dependent variable with an F-statistic of 56.212 and $p < 0.001$, accounting for 44.5% of the variance. Visits also significantly influence the dependent variable, with 6% of the variance explained ($p = 0.003$). The interaction between group and visit is significant ($p = 0.037$), explaining 4.6% of the variance.

2) Model 2 nWBV Scores by Group across visits - Mixed Effect ANOVA

Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	0.34	2	140	0.017	6.80	0.002	0.089	nan
Visit	0.07	1	140	0.007	97.52	<0.001	0.411	1.00
Interaction	0.00	2	140	0.000	1.79	0.171	0.025	nan

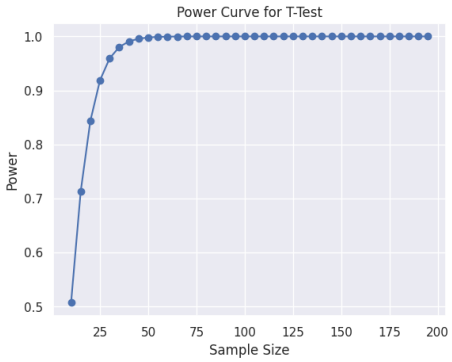
Interpretation: The Mixed Effects ANOVA shows that there are statistically significant differences between groups ($p = 0.002$) with a small to medium effect size, and across visits ($p < 0.001$) with a large effect size. However, the interaction between group and visit is not statistically significant ($p = 0.171$), indicating that the effect of the group does not vary over time.

5. Statistical Power Analysis

Sample Size	45.451 ≈ 46
Power	0.998

The result indicates that a sample size of approximately **46** participants per group is needed to detect an effect size of 0.7 with a power of 0.91 at a significance level of 0.05. The result is a power of approximately **0.998.**

Power Curve for T-test



Interpretation: The power curve for the t-test shown in the graph demonstrates a rapid increase in statistical power as sample size increases, particularly noticeable up to a sample size of 50. Beyond this point, the power gain diminishes and eventually plateaus close to a power of 1.0, indicating near certainty in detecting a true effect, around a sample size of 100. This suggests that a sample size between 50 to 100 is optimal for balancing the ability to detect an effect and the resources expended for data collection.

6. Assumption Check

1) a. Normality of residuals

Model 1(MMSE) Model 2 (nWBV)

Group	W	pval	normal	Group	W	pval	normal
Nondemented	0.8095	<0.01	False	Nondemented	0.9889	0.3170	True
Demented	0.9291	<0.01	False	Demented	0.9899	0.5012	True
Converted	0.7709	<0.01	False	Converted	0.9582	0.3580	True

Interpretation: The Model 1 residuals for each group do not follow a normal distribution, The Model 2 residuals for each group follow a normal distribution.

2) Homogeneity of variance –Levene's test result for homogeneity of variances

Model 1					Model 2			
	W	pval	equal_var			W	pval	equal_var
Levene	65.19	<0.01	False		Levene	0.936512	0.393175	True

Interpretation: For model 1, the Levene statistic (W) is 65.19. The p-value is extremely small. This means the assumption of equal variances is violated for Model 1. The column "equal_var" states "False," aligning with the p-value result. For model 2, the Levene statistic is 0.937, suggesting less variation between group variances. The p-value is 0.39, which is greater than 0.05, implying that there is not enough evidence to suggest that variances are unequal; thus, the assumption of homogeneity of variances is met for Model 2. The column "equal_var" states "True," aligning with the p-value result.

3) a. Sphericity (for within-subjects factor) – Model 1 (MMSE)

	Model 1	Model 2
Mauchly's test	(True, nan, nan, 1, 1.0)	(True, nan, nan, 1, 1.0)

Interpretation: For model 1, the True could indicate that the assumption of sphericity has been met. For model 2, the True could indicate that the assumption of sphericity has been met.

7. Conclusion

In conclusion, cognitive functioning, as quantified by MMSE scores, varies significantly across different visits for patients with dementia compared to those without, demonstrating a notable decline in cognitive abilities over time. This decline is further emphasized by the differential trajectory observed in the normalized Whole Brain Volume (nWBV) between the demented and non-demented groups. These findings confirm the progressive nature of dementia, characterized by a decrease in cognitive function and brain volume, which is significantly impacted by the disease's progression. The interaction between cognitive and neuroanatomical changes across visits highlights the intricate dynamics of dementia, underscoring the importance of early detection and the development of personalized treatment strategies tailored to individual progression patterns. The statistical analyses employed, particularly the mixed effect ANOVA, highlighted the importance of considering both within-subject variability and between-group differences in longitudinal studies. The power analysis further validated the robustness of the study design, ensuring a high likelihood of detecting true effects. Challenges such as non-normal distribution of residuals and violation of homogeneity of variances in some models prompted careful consideration and adjustments in the analysis approach. This study thus provides a comprehensive insight into the cognitive and neuroanatomical trajectories of dementia.

The report's findings underscore the critical importance of early detection and the potential for personalized treatment strategies in managing dementia. By demonstrating significant differences in cognitive decline and brain volume reduction between demented and non-demented individuals, it highlights the need for targeted interventions tailored to the specific progression patterns of each patient. Furthermore, the insights provided into the dynamics of dementia pave the way for future research, offering a solid foundation for studies aimed at unraveling the complex interplay between cognitive functions and neuroanatomical changes. This could lead to the development of innovative therapeutic approaches, ultimately improving the quality of life for individuals affected by dementia.